IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

AUXILIUM PHARMACEUTICALS, INC. and FCB I, LLC, Plaintiffs, v. UPSHER-SMITH LABORATORIES, INC., Defendant.	C.A. No. 13-148-SLR **REDACTED PUBLIC VERSION**

PLAINTIFFS' ANSWERING BRIEF IN OPPOSITION TO UPSHER-SMITH LABORATORIES, INC.'S MOTION FOR SUMMARY JUDGMENT (D.I. 26)

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EXPLANATION OF CITATION FORMS

- "ANDA action" refers to *Auxilium Pharms., Inc. v. Upsher-Smith Labs., Inc.*, No. 08-908-SLR (D. Del.) (case administratively closed December 13, 2011).
- "Compl." refers to Plaintiffs' Complaint for Patent Infringement, filed January 28, 2013 (D.I. 1).
- "Friend Decl." refers to the Declaration of David R. Friend, dated May 3, 2013.
- "Hadgraft Decl." refers to the Declaration of Jonathan Hadgraft, dated May 3, 2013.
- "Kennedy Decl." refers to the Declaration of Michael N. Kennedy, counsel for Auxilium, dated May 3, 2013.
- "*Orange Book*" refers to the FDA publication *Approved Drug Products with Therapeutic Equivalence Evaluations*.
- "Taavola Decl." refers to the Declaration of Lars P. Taavola, counsel for Defendant, dated April 5, 2013 (filed under seal, redacted versions filed as D.I. 34 (volume 1) and D.I. 35 (volume 2)).
- "USL" refers to Defendant Upsher-Smith Laboratories, Inc.
- "USL Br." refers to Defendant Upsher-Smith Laboratories, Inc.'s Opening Brief in Support of its Motion for Summary Judgment of Non-Infringement of the Patents-in-Suit, dated April 5, 2013.

I. INTRODUCTION AND NATURE AND STAGE OF PROCEEDINGS

Upsher-Smith's ("USL's") motion for summary judgment has proved to be the "experiment in futility" that concerned the Court when it invited USL to "put its money where its mouth is." (Kennedy Decl. Ex. 14 (3/7/13 Tr.) at 6:11; *see also* 7:19-20.) The numerous factual issues in this case have not gone away simply because USL for years has insisted that that the case can be decided on an issue of law. USL's motion remains ill-conceived and a waste of time and resources.

USL contends that Plaintiffs are precluded, by the doctrine of prosecution history estoppel, from asserting that USL's product infringes any of the patents-in-suit under the doctrine of equivalents. USL's motion, however, is unsupported by any expert declaration and does not even try to come to grips with the numerous factual issues that arise from its effort to apply prosecution history estoppel in this case. As demonstrated below and in the accompanying declarations, there are multiple genuine issues of material fact precluding summary adjudication of USL's prosecution history estoppel arguments.

[redacted]

There, as here, USL represented to the Court that the estoppel issues made this a "simple case" with "straightforward facts" that are "not in dispute" (USL Br. at 1, 4). The Court advised USL that it "would not permit such a motion unless the parties submit an agreed upon statement of facts, ensuring that the issue truly is a matter of law." (ANDA action, D.I. 121.) The Court's concern was well-founded: the issues presented by USL's motion are deeply factual. Not surprisingly, it proved impossible for the parties to agree on a statement of undisputed facts. (*See* 3/26/13 Ltr. from Plaintiffs to the Court at 2 (filed under seal).) Despite its failure to meet the Court's condition for making a summary judgment motion in the ANDA action, USL persists

in making essentially the same motion now, in a case that is even more complicated. For all of these reasons, both USL's motion and the "rush to judgment" strategy from which it arises are wholly improper, and this motion should be denied.

II. SUMMARY OF THE ARGUMENT

1. USL asserts that the doctrine of equivalents is barred by amendment-based estoppel. This form of estoppel, however, disclaims only equivalents that fall within the "territory between the original claim and the amended claim." *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 535 U.S. 722, 740 (2002) ("*Festo VIII*") (citation omitted). Here, the original claims of many but not all of the applications resulting in the patents-in-suit claimed methods of treatment using compositions containing a "Hsieh enhancer." This refers to a class of excipients known as penetration enhancers, which are used to help deliver an active ingredient through the skin in transdermal drug products such as the products at issue here. The issued claims of the patents-in-suit recite (depending on the patent) only one or a few specific species of Hsieh enhancers. However, there are numerous penetration enhancers *other than* Hsieh enhancers, and USL's accused product uses a combination of three of those non-Hsieh enhancers (*i.e.*, "USL's enhancer system"—which are not in the prior art) to perform the same function, in the same way, to achieve the same result as the Hsieh enhancers recited in the claims of the patents-in-suit. Thus, amendment-based estoppel simply does not apply here, because USL's equivalent is not within the territory surrendered by amendment. (*See* Part IV.A.1 below.)

2. Even if a presumption of surrender arises with respect to amendment-based estoppel, Plaintiffs can rebut that presumption by showing "that the alleged equivalent would have been unforeseeable at the time of the narrowing amendment." *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 344 F.3d 1359, 1368 (Fed. Cir. 2003) ("*Festo X*"). Here, the alleged equivalent, USL's enhancer system, is not taught in the prior art. Instead, to attempt to

show foreseeability, USL relies solely on one prior art reference (the "Dudley" patent, Taavola Decl. Ex. 41 (D.I. 35-4)), which separately mentions each component of USL's enhancer system as a possible candidate to use *individually* as a penetration enhancer. But, as Plaintiffs' expert explains, the state of the art of penetration enhancers remains unpredictable, and a skilled artisan would not have been able to foresee the equivalence of USL's enhancer system with the relevant limitation just because each enhancer in the system might be used individually in some other context. At a minimum, there are genuine issues of material fact regarding the level of skill of a person of ordinary skill and the state of the prior art precluding summary judgment. (*See* Part IV.A.2.a)

3. Plaintiffs can separately rebut the presumption of surrender by showing that the rationale of the narrowing amendment bore "no more than a tangential relation to the equivalent in question." *Festo X*, 344 F.3d at 1369. Here, the amendment upon which USL relies was not made for the purpose of excluding the equivalent in question, which is USL's three-component enhancer system utilizing only *non-Hsieh enhancers*; indeed, the amendment had nothing to do with excluding USL's equivalent. Rather, the amendment resulted from discussions with the Patent and Trademark Office Examiner to align the literal scope of the claims commensurate with the scope of the surprising results reported. That is, the resulting claims more closely match the composition of TESTIM, which is a commercial embodiment of the claims, and which showed surprising results over ANDROGEL, which is a commercial embodiment of the Dudley reference.[1] The amendment was not related to excluding equivalents, and certainly not USL's enhancer system. (*See* Part IV.A.2.b)

[1] If USL truly believed that its generic product is practicing the Dudley prior art reference, it presumably could have filed its Section 505(b)(2) application as a generic equivalent to ANDROGEL. Instead, USL filed its application as a purported generic equivalent to TESTIM, a different product, because USL recognizes that its formulation is *not the same* as the prior art.

4. For several reasons, argument-based estoppel does not apply here. Because the rationale for any narrowing amendments did not relate to the use of non-Hsieh enhancers at all, there was no "clear and unmistakable" disavowal of USL's equivalent, a combination of three non-Hsieh enhancers. Moreover, the prosecution history reflects no disavowal of claim scope, but rather Applicant's acquiescence in amendments demanded by the Examiner to meet the scope of demonstrated unexpected results. USL itself agrees that the amendments were required by the Examiner. But USL does not attempt to answer the question—because it cannot—of how *Plaintiffs* could be found to have disavowed subject matter. (*See* Part IV.B below.)

5. At minimum, prosecution history estoppel does not apply to two of the patents-in-suit, the '608 Patent and the '610 Patent. These patents are continuations of the '968 Patent, but their claims, both as originally filed and as issued, recite additional Hsieh enhancers beyond the single Hsieh enhancer (oxa-2-one) claimed by the '968 Patent. USL's brief glosses over the rule that prevents prosecution history estoppel from extending from a parent patent to continuations unless those continuation applications have *the same* relevant claim language. The language of the claims of '608 and '610 patents is different and was not amended during prosecution, leaving no basis for even a rebuttable presumption of estoppel. (*See* Part IV.C below.)

6. USL is also wrong in its argument that the doctrine of equivalents is always unavailable when claim limitations (such as the enhancer limitations in the patents-in-suit) recite specific chemicals (such as "oxa-2-one" or a group of specific Hsieh enhancers). USL again misstates the law relevant to this argument (including by its reliance on the inapposite *Wrigley* precedent), and ignores a genuine issue of material fact: whether the inventor made a deliberate decision to write narrow claims that exclude USL's unforeseeable equivalent. As with so many

of its arguments, not only does USL fail to demonstrate that this issue can be resolved without a trial, it does not acknowledge that the issue exists. (*See* Part IV.D below.)

III. STATEMENT OF FACTS

A. Plaintiffs created an innovative therapeutic testosterone gel product.

"Male hypogonadism" is a medical condition suffered by men who have below-normal concentrations of testosterone. (Compl. Ex. A ('968 Patent) at col. 1:59-63.) The symptoms of this condition can be reduced using testosterone replacement therapies, such as testosterone gels applied to the skin. (Kennedy Decl. Ex. 1 at 213.) To treat this condition, physicians can prescribe a gel product containing testosterone (the active ingredient) in combination with a number of excipients (inactive ingredients). Such gels are designed to deliver testosterone through the skin into the bloodstream. To facilitate this "transdermal" route of administration, testosterone gels typically include, among other ingredients, one or more inactive ingredients called "penetration enhancers" or simply "enhancers." An enhancer is a compound capable of modifying the rate of passage (called the "flux") of an active ingredient through the skin into the bloodstream. (Hadgraft Decl. ¶ 127.)

FDA approved the first testosterone gel product in 2000. This product, called ANDROGEL, contains 1% testosterone along with a number of inactive ingredients. (Kennedy Decl. Ex. 16 at 1.) ANDROGEL is a commercial embodiment of the invention claimed in a 2003 patent, U.S. Patent No 6,503,894, the "Dudley patent." (Taavola Decl. Ex. 41 (D.I. 35-4).)

TESTIM is the result of extensive research efforts to develop a testosterone gel product that would improve upon ANDROGEL. [redacted] Until its expiration in 2008, the Hsieh patent claimed a genus of enhancers known as

"Hsieh enhancers." Hsieh enhancers differ from other penetration enhancers by their distinctive structural formula. (*See* Friend Decl. ¶¶ 130-31.) According to the '968 patent, an advantage of Hsieh enhancers is that they "are lipophilic and are 'membrane-compatible,' meaning that they do not cause damage to the membrane on which the [] composition of the present invention is to be applied. . . . Such enhancers produce also a low level of irritability or no irritability to the target membrane and, in fact, serve as an emollient." (Compl. Ex. A at col. 7:2-7.)

Building on the Hsieh patent's technology, the inventor, Robert Gyurik, developed a testosterone gel formulation containing a Hsieh enhancer called oxacylcohexadecan-2-one (hereinafter, "oxa-2-one"). [redacted]

Auxilium's commercial product based on this formulation, TESTIM, was approved by FDA in October 2002. With this approval, Auxilium met its goal of improving upon ANDROGEL. Specifically, studies have shown that TESTIM is more effective than ANDROGEL at delivering testosterone into the bloodstream. Indeed, TESTIM is 30% more effective than ANDROGEL, when comparing two parameters—the C_{max} (maximum concentration of testosterone) and the $AUC_{0\text{-}24}$ (meaning "area under the curve," a measure of the amount of circulating testosterone over twenty four hours)—for hypogonadal males treated with the two products. (Taavola Decl. Ex. 1 (D.I. 34-1) at USL00271175.)

B. The TESTIM Orange Book patents.

The FDA-approved method of using TESTIM is covered by nine U.S. patents, and the TESTIM formulation itself is covered by a tenth patent, all listed in the *Orange Book* for TESTIM. The first, U.S. Patent No. 7,320,968 (the '968 Patent), issued on January 22, 2008,

from Application No. 10/473,724 (the "'724 Application").[2] The other nine patents-in-suit all resulted from continuation applications from the '968 Patent.[3] All ten patents-in-suit are currently owned by FCB I and exclusively licensed to Auxilium. (*See* Compl. ¶¶ 14-32.) As USL's prosecution history estoppel arguments focus almost entirely on prosecution of the '724 Application that led to the '968 Patent, a brief summary of that prosecution is set forth below.

The '724 Application originally contained 52 claims. These claims generally encompassed a pharmaceutical composition comprising an androgen and an enhancer useful for androgen delivery, a method of use of that composition, and a method of manufacture of that composition. (*See* Friend Decl., Appendix ¶ 2.) Before the application was substantively examined at the PTO, the Applicant made several preliminary amendments deleting, amending, and adding claims. (*Id.*) Over the course of those preliminary filings, the Applicant maintained the term "Hsieh enhancer" in its independent claims (either originally presented or added).

The '724 Application was pending for almost four years before the PTO issued its first Office Action on February 15, 2007. (*See* Friend Decl. ¶ 190.) In that Office Action, the Examiner rejected all claims for obviousness under 35 U.S.C. § 103, and for lack of enablement under 35 U.S.C. § 112. (*See* Kennedy Decl. Ex. 5 at 4-10.) As relevant here, the obviousness rejection was based on the Dudley patent in view of the Hsieh patent. In light of these references, the Examiner found it would have been "obvious to one of ordinary skill in the art at the time the invention was made, to modify the composition taught by Dudley to include the

[2] The '724 Application was a U.S. national phase application of Patent Cooperation Treaty international application serial number PCT/US03/12235, filed on April 21, 2003. Both applications claim priority to U.S. provisional patent application serial number 60/374,103, filed in the PTO on April 19, 2002. (*See* Friend Decl., Appendix ¶ 1.)

[3] These nine patents, all issued between 2009 and 2012, are 7,608,605 (the "'605 Patent"); 7,608,606 ("'606 Patent"); 7,608,607 ("'607 Patent"); 7,608,608 ("'608 Patent"); 7,608,609 ("'609 Patent"); 7,608,610 ("'610 Patent"); 7,935,690 ("'690 Patent"); 8,063,029 ("'029 Patent"); and 8,178,518 ("'518 Patent"). (*See* Compl. ¶¶ 15-32, *id.* Ex. B-J.)

enhancer taught by Hsieh." (*Id.* at 9.) Applicant responded to the Office Action on April 30, 2007. (*See* Taavola Decl. Ex. 1 (D.I. 34-1).) The Applicant cancelled numerous claims and added other claims. The broadest remaining claims, independent claims 40 and 85–88, continued to recite the element "Hsieh enhancer." (*See id.* at USL00271155-165.)

Interviews with the Examiner and her supervisors occurred on May 22, 2007 (Kennedy Decl. Ex. 6) and June 12, 2007 (Taavola Decl. Ex. 4 (D.I. 34-1)). In the June 12 interview, the Examiner proposed amending all claims to recite oxa-2-one as the enhancer, and stated that such claims would be allowable if this and other amendments were made. (Taavola Decl. Ex. 4 (D.I. 34-1).) Applicant explained that, in light of objective indicia of non-obviousness, Applicant did not believe it necessary to amend the claims. (*See* Friend Decl. ¶ 192.)

However, in light of the extraordinary delay in examining the '724 Application, combined with the approaching expiration of the only patent that then covered TESTIM (the Hsieh patent), the Applicant dropped its resistance to amending the pending claims. As explained by Plaintiffs' expert, Dr. David Friend:

> As confirmed by subsequent events in the prosecution history of the '724 Application, a reasonable competitor would understand that the looming threat of the expiration of the Hsieh '252 Patent compelled the Applicant to change course. The PTO's unexpected delay in starting to process the '724 Application had put immense time-pressure on the Applicant to secure patent protection. Any appeal of a rejection to the Board of Patent Appeals and Interferences would be expected to take several months or more. In addition, even after allowance of claims, other administrative steps including final application processing and printing of the patent could delay the ultimate issuance of the patent until after the June 2008 expiration of the Hsieh '252 Patent.

(Friend Decl. ¶ 193.) To expedite issuance, Applicant then filed a Supplementary Reply on July 19, 2007. (Taavola Decl. Ex. 5 (D.I. 34-1).) In this Reply, the Applicant acquiesced to the Examiner's demand to amend the claim limitation reciting Hsieh enhancers to instead recite a

species of Hsieh enhancer, oxa-2-one. The Applicant also added new claims which were likewise limited to the oxa-2-one element. This July 19, 2007 amendment is the primary amendment upon which USL relies for its prosecution history estoppel arguments.

The prosecution history clearly reflects that the July 19, 2007 amendment was made at the insistence of the Examiner as the only way to gain issuance of a patent. In its July 19 Remarks, the Applicant referenced the Summary from the June 12, 2007 Examiner Interview. The Applicant noted the Examiner's statement, "which indicates the allowability of the claims . . . if the claims are amended to define the composition which is referred to in the claims as containing [oxa-2-one] . . . and testosterone." (Taavola Decl. Ex. 5 (D.I. 34-1) at 9.)

A subsequent Interview with the Examiner took place on August 20, 2007, when the Examiner required still additional amendments. (Friend Decl. ¶ 198.) The Examiner's Summary of the Interview stated as follows: "Examiner recommended incorporation of glycerin, propylene glycol co-solvents and polyethylene glycol limitations to existing claims with limitations on testosterone, [oxa-2-one], thickening agent, and primary solvent." (Kennedy Decl. Ex. 7.) Under the circumstances, Applicant had no choice but to acquiesce.

The Examiner issued a Notice of Allowability and Examiner's Amendment on September 5, 2007. (*See* Friend Decl. ¶ 200.) The Examiner's Amendment provided the full text of the allowed claims, and reported that Applicant's attorney had, in a telephone call, authorized the Examiner to use the claims the Examiner had proposed. In the Examiner's accompanying statement of Reasons for Allowance, the Examiner stated:

> The prior art of Dudley teaches the use of a testosterone gel applied to the skin with certain enhancers. Hsieh teaches the genus of Hsieh enhancers and the specific enhancer [oxa-2-one], but does not suggest the specific combinations now claimed. The declarations go to the benefits of the specific combination of the instant formulation for use in hypogonadism such as the specific

> incorporation of testosterone with ethanol or isopropanol with glycerin and propylene glycol, the specific enhancer [oxa-2-one], and polyethylene glycol as a crystallization inhibitor in the ranges disclosed.

(Taavola Decl. Ex. 7 (D.I. 34-1).) The '968 Patent issued on January 22, 2008. Claim 1 of the patent is most relevant here, and recites, *inter alia*, the following:

> **1. A method for maintaining an effective concentration of testosterone in the blood serum of a male for treating hypogonadism which comprises transdermally delivering to the male by applying to the skin a composition which is in the form of a topical gel**, which has a viscosity of about 2000 to about 6000 cps and a pH of about 4 to about 8, **and comprises**: (A) about 0.1 to about 5 wt. % of testosterone; **(B) about 0.5 to about 15 wt. % of oxacyclohexadecan-2-one; (C)** about 1 to about 6 wt. % of a thickening agent; (D) a mixture of solvents which include: (i) about 60 to about 75 wt. % of ethanol or isopropanol; and (ii) propylene glycol and glycerin as co-solvents; and (E) about 0.001 to about 5% wt. % of polyethylene glycol as a crystallization inhibitor. . . .

(Compl. Ex. A ('968 Patent), cl. 1 (emphases added).) The other nine patents-in-suit (Compl. Ex. B-J) are all continuations of the '968 Patent. Five of these patents (the '605, '606, '607, '609, and '518 Patents) claim either methods of treatment using a composition containing oxa-2-one; or, in the case of the '518 Patent, such a composition itself. The other four patents (the '608, '610, '690, and '029 Patents) claim methods of treatment involving the use of a subset of five Hsieh enhancers. (*See* Friend Decl. ¶¶ 20-118.)

C. USL develops a generic version of TESTIM.

[redacted]

[redacted] Instead of oxa-2-one, this formulation contains USL's enhancer system comprised of three components: diisopropyl adipate, methyl laurate, and oleyl alcohol. As USL admits (USL Br. at 5, 12), none of the enhancers it uses is a Hsieh enhancer. (*See also* Friend Decl. ¶¶ 129-133, 164-166.)

Plaintiffs will show at trial that USL's formulation infringes claims of each of the asserted patents under the doctrine of equivalents, and specifically that USL's enhancer system is equivalent to oxa-2-one. Plaintiffs will show (1) that both oxa-2-one and USL's enhancer system perform substantially the same function—to act as enhancers and thus increase the rate of passage of an active ingredient (testosterone) through the skin; (2) that USL's enhancer system acts in substantially the same way as oxa-2-one in the claimed formulation; and (3) that USL's enhancer system achieves substantially the same result as oxa-2-one, delivering very similar amounts of testosterone. [redacted]

IV. ARGUMENT

USL seeks summary judgment of non-infringement primarily based on prosecution history estoppel. Prosecution history estoppel prevents a patentee from using the doctrine of equivalents to recapture subject matter that had been surrendered during prosecution. *See Warner-Jenkinson Co. v. Hilton Davis Chem. Co.*, 520 U.S. 17, 30 (1997). There are two ways that estoppel can arise. *First*, an applicant can surrender subject matter through a narrowing amendment to the claims (amendment-based estoppel). *See, e.g., Conoco, Inc. v. Energy & Envtl. Int'l, L.C.*, 460 F.3d 1349, 1363 (Fed. Cir. 2006). *Second*, an applicant can surrender subject matter through an argument made to the examiner (argument-based estoppel). *See id.*

In denying a motion for summary judgment on prosecution history estoppel grounds, this Court recently recognized that "the Supreme Court has rejected a per se approach in which a finding of estoppel would bar a patentee from later asserting a claim under the doctrine of equivalents regarding the narrowed element. Indeed, such a practice is 'inconsistent with the purpose of applying the estoppel in the first place—to hold the inventor to the representations made during the application process and to inferences that may reasonably be drawn from the amendment.'" *McKesson Automation, Inc. v. Swisslog Italia S.P.A.*, 712 F. Supp. 2d 283, 302-03 (D. Del. 2010) (Robinson, J.) (*quoting Festo VIII*, 535 U.S. at 738.).

The summary judgment standard is familiar to the Court.[4] In particular, summary judgment is properly denied where the party opposing summary judgment raises a genuine issue of material fact by proffering expert testimony in conflict with the positions of the moving party. *See, e.g., Metro. Life. Ins. Co. v. Bancorp Servs., LLC*, 527 F.3d 1330, 1339 (Fed. Cir. 2008) (holding the "conflict in [expert] declarations created a genuine issue of material fact that made summary judgment inappropriate"); *B-K Lighting, Inc. v. Fresno Valves & Castings, Inc.*, 375 Fed. App'x. 28, 32 (Fed. Cir. 2010) (nonprecedential) (same).

A. Amendment-based estoppel does not apply to any claim of any patent-in-suit.

In the case of amendment-based estoppel, "[a] patentee's decision to narrow his claims through amendment may be presumed to be a general disclaimer of the territory between the original claim and the amended claim." *Festo VIII*, 535 U.S. at 740. Even if this *Festo*

[4] A party is entitled to summary judgment when, viewing the record in the light most favorable to the non-movant, the record shows that there is no genuine issue as to any material fact and that the movant is entitled to judgment as a matter of law. *See, e.g., Montone v. City of Jersey City*, 709 F.3d 181, 189 (3d Cir. 2013) (citing Fed. R. Civ. P. 56(a)). "Facts that could alter the outcome are 'material,' and disputes are 'genuine' if evidence exists from which a rational person could conclude that the position of the person with the burden of proof on the disputed issue is correct." *Horowitz v. Fed. Kemper Life Assurance Co.*, 57 F.3d 300, 302 n.1 (3d Cir. 1995) (internal citations omitted).

presumption arises, the presumption can be rebutted in three ways: unforeseeability, tangentiality, or "some other reason." *Id.* at 740–41.

Here, USL's summary judgment motion as to amendment-based estoppel must be denied. *First*, USL's enhancer system does not even fall within the territory between the original claims of the '724 Application (which claimed Hsieh enhancers), and the issued claims of the '968 Patent and its continuation patents (which, depending on the patent, cover oxa-2-one or a handful of related Hsieh enhancers). *Second*, even if USL could somehow show that its equivalent *is* within the territory surrendered, there are disputed issues of material fact with respect to whether Plaintiffs can rebut any presumption of estoppel that might apply.[5]

1. USL's equivalent is not within the territory between the original claims of the '724 Application and the amended claims of the '968 Patent.

"A patentee's decision to narrow his claims through amendment may be presumed to be a general disclaimer of the *territory between the original claim and the amended claim*." *Festo VIII*, 535 U.S. at 740 (emphasis added); *see also Festo X*, 344 F.3d at 1367 (same). The Supreme Court has explained that "[t]here is no reason why a narrowing amendment should be deemed to relinquish equivalents unforeseeable at the time of the amendment *and beyond a fair interpretation of what was surrendered*." *Festo VIII*, 535 U.S. at 738 (emphasis added).

According to controlling precedent, amendment-based estoppel surrenders only equivalents that would have been literally covered by the original claim limitation but are not literally covered by the amended limitation. For example, in *Intervet v. Merial Ltd.*, a

[5] The amendment-based estoppel discussion in this Opposition focuses on the amendment made during prosecution of the '724 Application that led to the '968 Patent. To the extent USL contends that amendment-based estoppel applies to other amendments to "enhancer" limitations made during prosecution of certain continuation patents (*see* USL Br. at 19), such arguments should be rejected for the same reasons as apply to the '968 Patent.

presumption of surrender arose as to "all equivalents that reside in the territory between" a group of nucleotide sequences originally claimed and the smaller group claimed through amendment. 617 F.3d 1282, 1291-92 (Fed. Cir. 2010). However, there was no surrender with respect to the asserted equivalent, a nucleotide sequence not literally within the original claim language. *Id.*

Even cases applying amendment-based estoppel do so only after determining that the asserted equivalent in question actually fell within the territory between the original and the amended claims. In *Schwarz Pharma, Inc. v. Paddock Laboratories, Inc.*, the Federal Circuit held that "that the presumption of surrender applies to [the accused equivalent magnesium oxide] because it clearly falls within the territory between the language of the original and the amended claims." 504 F.3d 1371, 1376-77 (Fed. Cir. 2007). Under USL's theory, there would have been no need to specify that magnesium oxide fell within any "territory." Similarly, in *Pacific Coast Marine Windshields Ltd. v. Malibu Boats, LLC*, the court found estoppel only after "[c]omparing the [] accused design with the patented design and the canceled embodiments," and thus finding that "the accused design is within the territory between the original claim and the amended claim." 12-cv-33, 2012 WL 6721060, at *3 (M.D. Fla. Dec. 27, 2012).

Tellingly, USL's brief completely skips this step of the analysis, instead simply assuming any amendment to the enhancer limitations surrenders every conceivable penetration enhancer other than the ones recited in the issued claims of each Patent-in-Suit. (USL Br. at 18-20; *see also id.* at 1 (asserting that the amendment gave up "any and all equivalents to its special ingredient").) USL adopts this erroneous view of the law because it knows full well that its equivalent enhancer system falls outside the territory between the original claims of the '724 Application and the claims as amended during prosecution and issued in the '968 Patent.

All substantively examined independent claims of the '724 Application originally recited the phrase "Hsieh enhancer." (Kennedy Decl. Ex. 100 at USL0002901-909.) After the claims were amended during prosecution, the issued '968 Patent contained one independent claim, which claimed formulations with the enhancer "oxacyclohexadecan-2-one" ("oxa-2-one"). (*See* Compl. Ex. A ('968 Patent), cl. 1.) It is undisputed that oxa-2-one is a species of Hsieh enhancer. (*See, e.g.,* USL Br. at 5.) Thus, the "territory between the original claim and the amended claim," in terms of *Festo VIII*, logically cannot encompass penetration enhancers that are not Hsieh enhancers. 535 U.S. at 740. USL's brief admits as much.[6] And as USL also agrees (USL Br. at 12-13), there are many penetration enhancers that do *not* qualify as Hsieh enhancers. (*See also* Friend Decl. ¶¶ 129-133, 164-166.)

In light of these facts, USL's amendment-based estoppel argument is finished. None of the three enhancers used in combination in USL's formulation (diisopropyl adipate, methyl laurate, and oleyl alcohol) is a Hsieh enhancer, nor do they combine to form Hsieh enhancers in USL's testosterone gel formulation. (USL Br. at 5, 12; *see also* Friend Decl. ¶¶ 165-67.) Thus, USL's replacement enhancers do not fall within the territory between the claim language as originally written and the claim language as amended, and therefore could not have been surrendered. For this reason alone, any amendment-based prosecution history estoppel cannot bar a doctrine of equivalents claim in this case.[7]

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[6] *See* USL Br. at 6 (acknowledging that the Examiner concluded only that "not all *Hsieh enhancers* could be claimed" (emphasis added); *id.* at 8 (asserting that the patentee "surrendered a broader class of *Hsieh enhancers*" (emphasis added)).

[7] If anything, the undisputed facts identified above demonstrate that *Plaintiffs* are entitled to summary judgment in their favor that amendment-based estoppel does not apply in this action. *See* Fed. R. Civ. P. 56(f)(1) ("After giving notice and a reasonable time to respond, the court may . . . . (1) grant summary judgment for a nonmovant;"); *see also Hoffmann-La Roche Inc. v. Apotex Inc.*, 07-Civ-4417, 2012 WL 4661588, at *7-8 (D.N.J. Oct. 1, 2012).

2. Plaintiffs can rebut any presumption of amendment-based estoppel.

Even assuming *arguendo* that—contrary to the facts—USL's equivalent falls within the surrendered claim territory, summary judgment should still be denied because there are numerous genuine disputed issues of material fact concerning whether Plaintiffs can *rebut* the presumption of surrender. As noted above, there are three ways to rebut the presumption: (1) "[t]he [alleged] equivalent [would] have been unforeseeable at the time of the application," (2) "the rationale underlying the amendment [bears] no more than a tangential relation to the equivalent in question," or (3) "there may be some other reason suggesting that the patentee could not reasonably be expected to have described the insubstantial substitute in question." *Festo VIII*, 535 U.S. at 740–41. While the application of prosecution history estoppel is ultimately a question of law, this inquiry is based on underlying facts, and disputes concerning those facts preclude summary judgment. *See SmithKline Beecham Corp. v. Excel Pharm., Inc.*, 356 F.3d 1357, 1365 (Fed. Cir. 2004) ("[T]he present record does not address . . . foreseeability . . . at the time of the narrowing amendment. Thus, this record does not address whether Glaxo . . . rebutted the presumption of surrendered equivalents. . . . Because a material issue of fact remains . . . Excel was not entitled to summary judgment of noninfringement. . .").

As demonstrated below and in the accompanying declarations, there are material issues of fact with respect to at least two of the three grounds of rebuttal. USL barely addresses rebuttal of the alleged presumption (*see* USL Br. at 20), doubtless expecting to sandbag Plaintiffs by addressing these issues substantively for the first time in its reply. Regardless, USL's reply submission will at most confirm that there are numerous disputed issues of fact concerning rebutting the *Festo* presumption, which make summary judgment inappropriate.

a) USL's equivalent was unforeseeable at the time of amendment.

Plaintiffs can rebut the presumption of surrender of the matter between the original claim limitation and the amended claim limitation by showing "that the alleged equivalent would have been unforeseeable" at the time of the narrowing amendment. *Festo X*, 344 F.3d at 1367; "[A]n alternative is foreseeable if it is disclosed in the pertinent prior art in the field of the invention. In other words, an alternative is foreseeable if it is known in the field of the invention as reflected in the claim scope before amendment." *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 493 F.3d 1368, 1379 (Fed. Cir. 2007) ("*Festo XIII*"). Whether an equivalent would have been unforeseeable at the time of the amendment is an objective inquiry, determined from the perspective of one of ordinary skill in the art at the time of the amendment. *Festo X*, 344 F.3d at 1369. As foreseeability is a fact-intensive inquiry, the court may consider expert testimony and other extrinsic evidence. *See id.*; *see also SmithKline Beecham Corp.*, 356 F.3d at 1363 (same).

USL's strategy to show the lack of genuine issues of material fact appears to consist of ignoring fact issues altogether. For example, USL's brief contains no discussion of two of the underlying factual inquiries related to foreseeability: The level of skill of a person of ordinary skill in the art, and the state of the art at the time of the application and the relevant amendment. *See Festo X*, 344 F.3d at 1369 ("[b]y its very nature, objective unforeseeability depends on underlying factual issues relating to, for example, the state of the art and the understanding of a hypothetical person of ordinary skill in the art at the time of the amendment.").

As to the definition of a person of ordinary skill in the art, Plaintiffs' expert Dr. Jonathan Hadgraft has concluded, based on thorough consideration of relevant materials, that in the early to mid- to late-2000s (the time of the invention and the patent claim amendments), a person of ordinary skill in the art pertaining to the patents-at-issue would have: (1) held a bachelor's

degree in a field related to formulation, such as chemistry, chemical engineering, biology, pharmaceutical sciences, pharmacy or a similar field and had several years of industrial work experience in formulating drugs for topical or transdermal delivery; or (2) held a Master's degree in the same areas and had about two to three years industrial work experience in formulating drugs for topical or transdermal delivery; or (3) held a Ph.D. in the same areas and had about one to two years industrial work experience in formulating drugs for topical or transdermal delivery. (*See* Hadgraft Decl. ¶¶ 117-125.) Notably, Dr. Hadgraft arrived at a different definition of person of ordinary skill in the art than that adopted by the Examiner. (*Id.* ¶ 119.) USL's motion, by contrast, makes no attempt to define a person of ordinary skill in the art despite acknowledging the centrality of a "person of ordinary skill in the art" (and the related concept of a "reasonable competitor") to the questions presented by USL's motion.[8] (*See* USL Br. at 15, 20.)

As to the state of the art, Dr. Hadgraft again was required to consider numerous factual and scientific issues, including the challenges of achieving effective transdermal delivery of a drug through the skin (Hadgraft Decl. ¶¶ 126-127), the properties and operation of penetration enhancers (*id.* ¶¶ 128-132), the failures in the art over a period of decades to develop more than a relative handful of drugs delivered transdermally (*id.* ¶¶ 133-135), and the unpredictability inherent in the art of penetration enhancers (*id.* ¶¶ 136-144). As a result of considering all of

[8] [redacted]

these issues, Dr. Hadgraft reached his conclusion that USL's enhancer system was undisclosed in the art at the time of the invention, and was thus unforeseeable as an equivalent to oxa-2-one. (*Id.* ¶¶ 150-168.) USL's motion is unaccompanied by *any* expert testimony, and USL makes no attempt to grapple with any of the issues identified by Dr. Hadgraft, much less demonstrate how foreseeability can be resolved on a paper record.

In any event, USL has failed to demonstrate that *the combination* of USL's replacement enhancers is even disclosed in the prior art. [redacted] Indeed, USL's opening brief nowhere contends that its combination of enhancers was known in Dudley (or other prior art), despite misleadingly implying that its generic product is practicing the prior art because it uses enhancers mentioned in Dudley. (*See* USL Br. at 12-13.) However, "a court must use the same definition of the equivalent to evaluate both foreseeability and infringement." *Honeywell Int'l, Inc. v. Hamilton Sundstrand Corp.*, 523 F.3d 1304, 1313 (Fed. Cir. 2008). For this reason, pointing to one prior art reference disclosing the three enhancers used individually still leaves USL far from demonstrating that the *combination* was a foreseeable equivalent to oxa-2-one or any other claimed Hsieh enhancer. *See, e.g., BEI Techs., Inc. v. Matsushita Elec. Indus. Co.*, 268 F. Supp. 2d 782, 800-02 (E.D. Mich. 2003) (equivalent was not foreseeable because it was "qualitatively different than what went before" in the prior art).

Even if (despite the lack of direction from the prior art) a skilled artisan had tried to combine USL's three-component enhancer system, it still would have been unforeseeable that doing so would have created an equivalent to oxa-2-one. For one thing, the subject area of penetration enhancers is inherently unpredictable and complex. For example, it is, and was at the time of the amendment, impossible to predict if a particular formulation containing the combination of diisopropyl adipate, methyl laurate, and oleyl alcohol (or any other combination) would enhance or retard the penetration of testosterone. (Hadgraft Decl. ¶ 136-138; *see also id.* ¶ 153.) Dr. Hadgraft explains that "it is and was impossible to predict with any degree of certainty whether combining multiple enhancers would result in an undesired effect and inhibit, rather than promote, transdermal drug delivery, as the combination of certain enhancers has been shown to inhibit the penetration of an active ingredient . . . . In addition, negative synergy is possible when multiple penetration enhancers are combined." (*Id.* ¶ 137; *see also id.* ¶ 150.) Even today, it is impossible to predict whether a specific formulation containing a penetration enhancer, including other inactive ingredients, will achieve effective transdermal drug delivery. (*Id.* ¶¶ 133-144.) Nor does it necessarily follow that, because an enhancer behaves in a certain way in one formulation, it will work in the same way in another formulation. (*Id.* ¶ 151.) Thus, it would have been unforeseeable to a skilled artisan at the time of amendment that USL's enhancer system would have worked in the same way as oxa-2-one in the composition claimed by the patents-in-suit. (*Id.* ¶¶ 150-154.)

The unpredictability in the relevant art was expressly recognized during prosecution of the '724 Application—as Applicant's expert declarant Dr. Kenneth Walters explained:

> [T]he mechanism by which compounds interact to increase the permeability of human skin to an active compound is extremely complex and not well understood. . . . [J]ust because one enhancer has been shown to increase the permeability of an active

> compound, there is no guarantee that another enhancer will increase the permeability of the same compound to the same extent as the first enhancer. The success of a particular transdermal formulation is dependent upon the specific skin permeation enhancer, at a specific concentration, in a specific formulation.

(Taavola Decl. Ex. 22 (D.I. 35-1) at 2; *accord* Hadgraft Decl. ¶¶ 136-142.) During prosecution of the '029 Patent, a continuation of the '968 Patent, the Examiner likewise expressly recognized the unpredictability of penetration enhancers. (Hadgraft Decl. ¶ 168.) The Examiner considering the application that became the '029 Patent stated that "[t]he art is unpredictable as even a change in the ring size of a particular compound core can materially affect its penetration capacity, wherein a change in a core such as the types of substitution would be more unpredictable." (Taavola Decl. Ex. 17 (D.I. 35-1) at 4.)

The unpredictability in the relevant art is confirmed by the subject matter disclosed in the '968 Patent. [redacted] In direct contrast to this data, the '968 Patent, and the TESTIM embodiment in particular, show that oxa-2-one in combination with other compounds can increase the permeation of testosterone in a given testosterone gel formulation. (*See* Hadgraft Decl. ¶¶ 155-167.)

[redacted]

[redacted]

For all of these reasons, a person of ordinary skill in the art could not foresee that USL's formulation, which employs a combination of three penetration enhancers in specific amounts, would produce similarly surprising results as the enhancers recited by the patents-in-suit, which are (depending on the patent) either oxa-2-one or one of a list of Hsieh enhancers. (Hadgraft Decl. ¶¶ 150-168.) Indeed, the similarity of the function, way, and result of USL's and the claimed formulations means that USL's is precisely the kind of equivalent intended to be embraced by the doctrine of equivalents. Accordingly, because the equivalent in question was

[9] Bioequivalence-related data can be relevant to the infringement inquiry, *see Abbott Labs. v. TorPharm, Inc.*, No. 97 C 7515, 2003 WL 22462614, at *19 (N.D. Ill. Oct. 29, 2003) (denying motion *in limine* and finding that statements made in ANDA were relevant to infringement).

not known in the prior art, and because USL provides no other basis to conclude that the equivalent was foreseeable, there is at a minimum a genuine issue of fact precluding summary judgment.[10]

b) The amendment at issue was tangential to the equivalent.

Separately, Plaintiffs can rebut any presumption of surrender by showing that "the rationale underlying the amendment bear[s] no more than a tangential relation to the equivalent in question." *Festo VIII*, 535 U.S. at 740–41. Whether the rationale for the amendment is tangentially related to an equivalent "necessarily requires focus on the context in which the amendment was made." *Festo X*, 344 F.3d at 1370. In order to determine whether the rationale for the narrowing amendment was tangential to the equivalent in question, a court will determine whether "the narrowing amendment was peripheral, or not directly relevant, to the alleged equivalent." *Id.* at 1369. Although a determination of tangentiality is made on the basis of the prosecution history, the district court may hear testimony from experts as to the proper interpretation of the prosecution history. *Id.* at 1370.

Here, the July 19, 2007 amendment upon which USL relies was not made to distinguish USL's equivalent—an equivalent which, as demonstrated above, was not even disclosed in the prior art. *Cf. Festo X*, 344 F.3d at 1369 ("[A]n amendment made to avoid prior art *that contains*

[10]At least because USL's enhancer system was not disclosed in the prior art, this case stands in stark contrast to recent Federal Circuit cases rejecting foreseeability arguments. For example, in *Duramed Pharmaceuticals, Inc. v. Paddock Laboratories, Inc.*, it was established that the prior art disclosed the use of the alleged equivalent in the relevant field of pharmaceutical compositions, but the Court rejected the proposition that foreseeability also required that the equivalent be known to be suitable for its intended purpose. 644 F.3d 1376, 1381-82 (Fed. Cir. 2011). And in *Schwarz Pharma*, the Court similarly found the alleged equivalent foreseeable simply because it was "known as a stabilizer in the field of pharmaceutical compositions," without requiring a further showing that the alleged equivalent was known as useful for the particular purpose claimed by the patents at issue. 504 F.3d at 1377. But here, the issue is not whether the alleged equivalent was known to be *useful*. Rather, USL has pointed to *no* prior art, nor put forward *any* expert testimony tending to establish that USL's enhancer system was known in *any* field relevant to the invention.

the equivalent in question is not tangential." (emphasis added)). Rather, as is clear from the prosecution history of the patents-in-suit, the reason for the amendments was to satisfy the Examiner's continued insistence that the claims be commensurate in literal scope with the data showing unexpected results. (*See* Friend Decl. ¶¶ 209-211.)

During prosecution of each of the patents-in-suit, the Applicant demonstrated through numerous expert declarations and experimental data that, compared to ANDROGEL, a testosterone gel formulation including the enhancer(s) recited by the '724 Application claims provided surprising and unexpected results, yielding highly effective testosterone delivery into the blood serum. (Friend Decl. ¶ 209.) For example, during prosecution of the '724 Application that led to the '968 Patent, the Applicant demonstrated that TESTIM produced a 30% greater mean "area under the curve" than ANDROGEL (the commercial embodiment of the Dudley patent). (Taavola Decl. Ex. 1 (D.I. 34-1) at 20-22; *id.* Ex. 22 (Walters Decl.) ¶ 20.) The Applicant argued that these results were surprising, and that a "skilled artisan would not have had any expectation" that such results would be achieved by combining Dudley to include a Hsieh enhancer. (Taavola Decl. Ex. 1 (D.I. 34-1) at 22.)

In response to this evidence, the Examiners consistently maintained rejections where the Examiners asserted that Applicant's claims were not commensurate in literal scope with the evidence of unexpected results. (*See* Friend Decl. ¶ 209.) The Applicant amended its claims in the patents-in-suit as the Examiners required, reciting only enhancers for which the data submitted provided evidence of unexpected results. (Friend Decl. ¶ 210.) For example, with respect to the '968 Patent, the Examiner required the Applicant to recite only oxa-2-one as the enhancer element, because the evidence of surprising results available at the time related to oxa-2-one. (*Id.* ¶ 211.) In contrast, in some of the continuation patents, other evidence demonstrated

that formulations including additional Hsieh enhancers produce comparable unexpected results. (*Id.*) As Plaintiffs' expert Dr. Friend explains:

> Because the amendments were made so that the scope of the claims would be commensurate with the unexpected results, a person of ordinary skill would also understand that the exclusion of any non-Hsieh enhancers or combinations of non-Hsieh enhancers is tangential to the reason for the amendment. Thus, a person of ordinary skill would conclude that the reason for the amendments . . . is tangential to the USL combination of enhancers that is the equivalent in question in this case.

(*Id.* ¶ 212.) With the purpose of the amendment being to align the scope of the claims with the unexpected results shown by certain Hsieh enhancers, the similarities between USL's enhancer system and the claimed enhancer systems means that it is precisely the kind of equivalent intended to be embraced by the doctrine of equivalents. This provides an additional, independent reason to deny USL's motion for summary judgment on amendment-based estoppel grounds. *See McKesson*, 712 F. Supp. 2d at 303 (denying summary judgment, concluding that the relevant amendment was tangential because patent was allowed in response to subsequent, unrelated amendment).[11]

B. Argument-based estoppel does not apply to any claim of any patent-in-suit.

USL also contends that, by distinguishing the Dudley patent and highlighting the benefits of its inventive formulation, Plaintiffs are precluded by argument-based estoppel from asserting the doctrine of equivalents over any enhancer other than those literally claimed in the patents-in-suit. (USL Br. at 20-22.) "To invoke argument-based estoppel . . . the prosecution history must evince a clear and unmistakable surrender of subject matter. Unlike amendment-based estoppel, [a court] do[es] not presume a patentee's arguments to surrender an entire field of equivalents

[11] For the reasons discussed further *infra* at Part IV.B.3, there is also "some other reason suggesting that the patentee could not reasonably be expected to have described the insubstantial substitute in question." *Festo VIII*, 535 U.S. at 741.

through simple arguments and explanations to the patent examiner." *Conoco*, 460 F.3d at 1364 (internal citations and quotation omitted). Argument-based estoppel applies only when a skilled artisan, viewing the question from the perspective of a competitor in the marketplace, would believe that the patent applicant surrendered the relevant subject matter. *Cordis Corp. v. Medtronic AVE, Inc.*, 511 F.3d 1157, 1177 (Fed. Cir. 2008).[12] Here, for several reasons, the file history decisively refutes any notion that there was a clear and unmistakable disavowal of USL's equivalent three-component enhancer system. (*See generally* Friend Decl. ¶¶ 168-206.)

1. Plaintiff did not clearly and unmistakably surrender every penetration enhancer listed in Dudley, much less USL's three-component enhancer system, which is not even disclosed in Dudley.

There can be no disavowal of USL's equivalent because, as discussed above (*supra* Part IV.A.2.a), the prosecution histories are devoid of references to the equivalent in question, which is the combination of diisopropyl adipate, methyl laurate, and oleyl alcohol acting as a penetration enhancer system in USL's testosterone gel formulation. Nor does the Dudley patent suggest that any of its laundry list of enhancers used individually would be equivalent to the claimed enhancer when used in combination. (*See* Friend Decl. ¶¶ 173-74; *see also supra* Part IV.A.2.a).) Thus, USL's argument that Applicant's references to Dudley surrendered "*any* formulation that does not include oxa-2-one or the other listed macrocyclic Hsieh enhancers," (USL Br. at 20 (emphasis added)) is both contrary to the record and contradicted by Federal Circuit law, which restricts the scope of any argument-based estoppel to the particular equivalent(s) that are the subject of the argument in question. *See Conoco*, 460 F.3d at 1355-56,

[12] USL acknowledges that, in this analysis, "the Court must examine the prosecution history as a whole" (USL Br. at 15), yet USL did not bother to submit the entire prosecution histories with its motion. (*See* Kennedy Decl. Ex. 100-109; *see also id.* Ex. 110-111.)

1364 (prosecution statement distinguishing formulations containing metal stearates did not estop plaintiff from arguing that C30+ wax was an equivalent, because C30+ was not a metal stearate).

The overbroad nature of USL's argument is further demonstrated by the fact that two of the enhancers mentioned in Dudley's laundry list (propylene glycol and polyethylene glycol) are *recited as excipients in several claims of the patents-in-suit*. (*See, e.g.,* Compl. Ex. A ('968 Patent), cl. 1; *see also* Friend Decl. ¶ 170.) The specifications of the patents-in-suit even refer to propylene glycol individually as a possible permeation enhancer. (*See, e.g.*, Kennedy Decl. Ex. 1 ('968 Patent), col. 9:1-3.) USL's argument thus requires this Court to find that the Applicant disavowed the use of ingredients it actually claimed. This is nonsense.[13]

2. The prosecution of continuations of the '968 Patent refute the notion that Applicant disavowed USL's equivalent during prosecution of the '724 Application.

The ongoing prosecution of continuation applications descended from the '968 Patent further refutes the notion that Applicant disavowed USL's equivalent. (Friend Decl. ¶¶ 175-77.) A pending claim in one of these continuations recites, in relevant part, "[a] method for maintaining a therapeutically effective concentration of testosterone in the blood serum of a male for treating hypogonadism which comprises . . . (B) about 0.01 to about 25 wt. % of at least one enhancer having a partition coefficient ranging from about 2.0 to about 9.0." (*Id.* ¶ 175.) This limitation is based on the same specification as the patents-in-suit and recites an enhancer *not limited* to the chemical structure of the enhancer. Thus, this limitation would encompass Hsieh and non-Hsieh enhancers whose partition coefficient fell within the recited range. (*Id.* ¶¶ 176-77.) Plaintiffs' expert Dr. Friend, reviewing the prosecution history from the perspective of the ordinarily skilled person, concluded that Applicant's continued pursuit of claims not limited to

[13] Other statements and actions in the prosecution histories of the patents-in-suit refute the notion that there was a disavowal. (Friend Decl. ¶¶ 175-205.)

Hsieh enhancers further undercuts USL's contention that Applicant clearly and unmistakably disavowed formulations that did not include Hsieh enhancers during prosecution of the parent '724 Application. (*Id.* ¶ 177.)

Similarly damaging to USL's disavowal contention is the fact that Applicant was able to claim in continuation patents (the '608, '610, '690, and '029 Patents) at least some of the subject-matter (*i.e.*, a broader selection of Hsieh enhancers in addition to oxa-2-one) that USL claims was clearly and unmistakably disavowed during prosecution of the '968 Patent.[14] (Friend Decl. ¶ 182.) As Dr. Friend confirms, a reasonable competitor would understand that it is customary practice for an applicant to obtain narrow claims in a parent and seek broader claims in continuations. (Friend Decl. ¶ 182.) If, however, the Applicant here had clearly and unmistakably disavowed all enhancers aside from oxa-2-one, the PTO would not even have permitted Applicant to pursue or obtain coverage over additional enhancers in the continuation applications. Put another way, under USL's argument, none of these continuation patent applications should contain any claims that reach more broadly than oxa-2-one. At a minimum, this argument presents yet another fact issue: Whether the filing and prosecution of numerous continuations of the '724 Application, seeking coverage of additional enhancers beyond oxa-2-one, objectively reflects Applicant's alleged disavowal of all enhancers aside from oxa-2-one.

[14] For the reasons explained by Dr. Friend, and contrary to USL's suggestion, the filing of terminal disclaimers during prosecution of the continuation applications would not suggest to a reasonable competitor that Applicant intended to disavow subject-matter. (Friend Decl. ¶ 183.) As is clear from the face of those disclaimers, they were filed to overcome obviousness-type double patenting rejections, not in order to disavow any particular subject-matter. Indeed, Applicant specifically noted that terminal disclaimers were being filed to expedite prosecution without conceding that the Examiner's rejection was proper.

3. The prosecution history shows that Applicant did not disavow enhancers other than oxa-2-one through acquiescence in the amendments demanded by the Examiner.

"[I]t is the applicant, not the examiner, who must give up or disclaim subject matter that would otherwise fall within the scope of the claims." *Innova/Pure Water, Inc. v. Safari Water Filtration Sys., Inc.*, 381 F.3d 1111, 1124 (Fed. Cir. 2004). Here, a reasonable competitor reviewing the prosecution histories along with other publicly-available information would recognize that the amendments during the '724 Application upon which USL relies did not constitute a disavowal by the Applicant of USL's equivalent three-component enhancer system. Instead, the course of prosecution with the Examiner resulted in amendments that altered the literal scope of the claims, but did so in a manner consistent with the purpose of aligning that scope with the unexpected results shown by the Applicant. But Applicant certainly did not disavow equivalents of the literal scope of the claims by making such amendments. At the same time, the Applicant pursued a common strategy (which it continues to pursue today) to obtain broader claims through a succession of continuation patents. (*See* Friend Decl. ¶ 175-177, 182.)

The prosecution history makes clear that it was the Examiner, not the Applicant, proposed amending all claims to include the specific Hsieh enhancer oxa-2-one and reciting "testosterone" instead of "androgen," and stated that such claims would be allowable "if in appropriate form and content." (Friend Decl. ¶ 192; *see also* Taavola Decl. Ex. 4 (D.I. 34-1) at 3.) To expedite the progress of prosecution, and specifically referencing the Examiner's statement concerning allowability, the Applicant amended its claims to recite oxa-2-one and testosterone on July 19, 2007, and also submitted declarations providing evidence of nonobviousness. (Friend Decl. ¶ 194.) Even after these amendments, which the Examiner had previously stated would make the claims allowable, the Examiner—not the Applicant—required further limitations to be added to the claims before she would allow them. (*Id.* ¶ 198.)

A reasonable competitor would conclude from a review of the '968 Patent prosecution history as a whole that the Applicant merely acquiesced in the Examiner's insistence that claims be limited. (Friend Decl. ¶¶ 184-206.) Nowhere is there any clear and unmistakable disavowal of subject matter outside the literal scope of the amendment required by the Examiner. Thus, USL cannot show argument-based estoppel through reliance on the Examiner's determination that the claims required amendment from "Hsieh enhancers" to "oxa-2-one." *See, e.g., Schwing GmbH v. Putzmeister Aktiengesellschaft*, 305 F.3d 1318, 1324-25 (Fed. Cir. 2002) ("[A]lthough prosecution history can be a useful tool for interpreting claim terms, it cannot be used to limit the scope of a claim unless the applicant took a position before the PTO that would lead a competitor to believe that the applicant had disavowed coverage of the relevant subject matter.").

4. Applicants' showing that the claimed invention exhibited unexpected results does not constitute a disavowal of USL's equivalent.

Contrary to USL's bald assertions (USL Br. at 11, 21), the demonstration during prosecution of the '724 Application that TESTIM exhibits unexpected results compared to ANDROGEL does not effect a disavowal of all formulations not containing oxa-2-one. For the same reasons, the showing of unexpected results arising from use of the other recited macrocyclic enhancers during prosecution of continuation applications does not effect a disavowal of other enhancers.

USL's brief does not directly quote the Walters Declaration (Taavola Decl. Ex. 22 (D.I. 35-1)) upon which it relies for the argument that Applicant's showing of unexpected results constitutes a disavowal. And for good reason, as USL's argument wholly depends on its blatant misreading of Dr. Walters's opinions. Dr. Walters stated in pertinent part that "it would have been unexpected to one of skill in this field that such a combination of active compound (testosterone) and enhancer ([oxa-2-one]) in the formulation disclosed in the present application

would result in a 30% increase in each of C_{max} and AUC_{0-24} of total testosterone (T) as compared to the ANDROGEL formulation." (Taavola Decl. Ex. 22 (Walters Decl.) ¶ 20 (D.I. 35-1).) Contrary to USL's representations (USL Br. at 21), Dr. Walters made no statement concerning the "singularity" or "uniqueness" of oxa-2-one; in particular he did not state that *only* oxa-2-one could possibly lead to the improved performance compared to ANDROGEL. Moreover, contrary to USL's contention, Dr. Walters did not compare oxa-2-one to *each and every* enhancer disclosed in Dudley, but rather to the enhancer used in ANDROGEL, one of the hundreds of enhancers disclosed in Dudley. For these reasons, Dr. Walters' declaration, and the Applicants' arguments based on his opinions, would not be read by a reasonable competitor to have disclaimed any and all equivalents—such as USL's three-component enhancer system—that exhibit the same improved performance compared to ANDROGEL.[15]

The sole case upon which USL relies for this argument is wholly inapposite. In *AstraZeneca UK Ltd. v. Dr. Reddy's Laboratories* (cited at USL Br. at 21), the court found an argument-based estoppel based on Federal Circuit cases where the patentee had stressed the singularity or uniqueness of the invention compared to the prior art. No. 08-3237-MLC, 2010 WL 4721384, at *7-8 (D.N.J. Nov. 15, 2010) (citing *Forest Labs., Inc. v. Abbott Labs.*, 239 F.3d 1305, 1313-14 (Fed. Cir. 2001) (disclaimer when patentee stated "'that *only* a surface-active material having the [claimed] chemical composition" exhibits unexpected results); *PODS, Inc. v. Porta Stor, Inc.*, 484 F.3d 1359, 1367-68 (estoppel when patentee referred to the claimed

[15] USL's reading of the '724 Application file history is further refuted by the fact that the Applicant showed during prosecution of several of the continuation patents that oxa-2-one did not actually possess "singular" properties. Specifically, the Feldman Declaration submitted by Applicant showed that additional Hsieh enhancers produce similar results to oxa-2-one and better results than ANDROGEL. (*See* Friend Decl. ¶ 204; *see also, e.g., id.*, Appendix ¶¶ 65, 71; Kennedy Decl. Ex. 104 at CPEX0115380-88.) As with the Walters Declaration, the Feldman Declaration likewise does not rely on the "singular" or "unique" properties of the claimed enhancers, thus refuting USL's citation-free argument that these results worked a disavowal of other enhancers in the '690, '029, and '518 Patents (USL Br. at 21).

"*singular* rectangular-shaped frame") (emphases added)). *AstraZeneca*'s holding was likewise based on prosecution statements that the unexpected results arose from "the one" dosage where the claimed ingredient was included. *Id.* at *9. There are no similar statements here.

There is no *per se* rule that an applicant always effects a disclaimer merely by reporting surprising results. For example, one district court found no estoppel arising from the argument that "an alkali or alkaline earth metal carbonate is a necessary ingredient," explaining that Federal Circuit precedent finds argument-based estoppel only when two facts are present: (1) statements that a feature is "critical," "unique," "superior," or "key," *coupled with* (2) arguments "that a potential equivalent to the particular aspect was 'not ... desired,' 'unworkable,' 'not ... easily and readily manufacturable,' or a 'disadvantage.'" *Schwarz Pharma, Inc. v. Paddock Labs., Inc.*, No. 05-832, 2006 WL 3004200, *2-4 (D. Minn. Oct. 20, 2006) (*citing Bayer AG v. Elan Pharm. Research Corp.*, 212 F.3d 1241, 1252-54 (Fed. Cir. 2000); *Pharmacia & Upjohn Co. v. Mylan Pharm., Inc.*, 170 F.3d 1373, 1377-78 (Fed. Cir. 1999); *Texas Instruments, Inc. v ITC*, 988 F.2d 1165, 1174-75 (Fed. Cir. 1993)). USL does not and cannot point to any statement in the prosecution history regarding its particular three-component enhancer system, let alone any statement suggesting that its enhancer system is unworkable. Like all of USL's efforts to find a disavowal of its enhancer system, this one fails.

* * *

For all of these reasons, the branch of USL's motion seeking summary judgment on argument-based estoppel is wholly contrary to the conclusion a reasonable competitor would draw from reviewing the prosecution histories of the patents-in-suit. There was no clear and unmistakable disavowal of coverage over USL's equivalent enhancer system.

C. At minimum, prosecution history estoppel does not apply to the claims of the '608 and '610 Patents, which recite different enhancers than the '968 Patent.

The claims of the '608 and '610 Patents, both in the original form and as issued, claimed several Hsieh enhancers. (Friend Decl. ¶¶ 49-57, 71-88; *id.* Appendix ¶¶ 44, 62.) That is, neither patent's prosecution histories features any amendments limiting the identity of the enhancers that could be used, and both of these patents issued with claims reciting additional Hsieh enhancers beyond oxa-2-one. Thus, contrary to USL's superficial analysis (USL Br. at 9, 19), any argument-based or amendment-based estoppel allegedly arising from the '724 Application cannot apply to the '608 Patent or '610 Patent.

"[T]he prosecution of one claim term in a parent application will generally not limit different claim language in a continuation application." *Invitrogen Corp. v. Colntech Labs., Inc.*, 429 F.3d 1052, 1078 (Fed. Cir. 2005) (interpreting the term "substantially reduced" without regard to the prosecution history of the term "substantially no" that was canceled in a preliminary amendment). Here, especially with respect to amendment-based estoppel, it would be illogical to apply the '724 Application's amendment and arguments concerning enhancers to the '608 Patent or '610 Patent, as those patents issued with claims literally covering several of the Hsieh enhancers that, according to USL, were "surrendered" in the '724 Application. *Cf. Saunders Grp., Inc. v. Comfortrac, Inc.*, 492 F.3d 1326, 1332-33 (Fed. Cir. 2007) (no prosecution disclaimer when relevant limitation of child patent was broader than limitation in parent application to which the alleged "disclaimer" relates).[16]

Nor can USL attempt to support its argument from the fact that terminal disclaimers were filed as to the '608 Patent and '610 Patent. (*See* USL Br. at 19 (appearing to assert that

[16] The case upon which USL relies is not to the contrary, as it applied argument-based estoppel to claims in later-issued patents that contained *the same* "self-erecting" limitation as the parent. *See Augustine Med. Inc. v. Gaymar Indus, Inc.*, 181 F.3d 1291, 1301 (Fed. Cir. 1999).

amendment-based estoppel should apply because "[t]he patents-in-suit are not patentably distinct from the claims of the parent patent, which was narrowly limited to compositions comprising [o]xa-2-one.").) The Federal Circuit has held that "the filing of a terminal disclaimer simply serves the statutory function of removing the rejection of double patenting, and raises neither presumption nor estoppel on the merits of the rejection." *Quad Envtl. Techs. Corp. v. Union Sanitary Dist.*, 946 F.2d 870, 874 (Fed. Cir. 1991). For these additional reasons, no estoppel can arise as to any claim of the '608 Patent or '610 Patent.

D. *Wrigley* does not preclude application of the doctrine of equivalents.

There is also no merit to USL's argument that, because the patents-in-suit literally claim only certain Hsieh enhancers, Plaintiffs are now "foreclosed from arguing that the patent can be expanded by resort to the doctrine of equivalents to include compounds in USL's formulation that are neither cyclic nor Hsieh enhancers." (USL Br. at 22.) USL appears to believe that, simply because its combination of three enhancers is neither disclosed nor literally claimed in the patents-in-suit, that combination is automatically *excluded* as an equivalent. Such an argument, if accepted, would of course abolish the doctrine of equivalents. *See Ethicon Endo-Surgery, Inc. v. U.S. Surgical Corp.*, 149 F.3d 1309, 1317 (Fed. Cir. 1998) ("[A]ny analysis of infringement under the doctrine of equivalents necessarily deals with subject matter that is 'beyond,' 'ignored' by, and not included in the literal scope of a claim.")

Moreover, the *Wrigley* precedent upon which USL relies is completely inapposite. (*See* USL Br. at 22-25 (citing *W.M. Wrigley Jr. Co. v. Cadbury Adams USA LLC*, 683 F.3d 1356 (Fed. Cir. 2012)). In fact, *Wrigley* is as different from the facts of this case as two cases can be. In *Wrigley*, the patent in question claimed use of a cooling agent called WS-3, and the asserted equivalent was a compound called WS-23, both of which were disclosed in the same prior art references as suitable substitutes for a cooling agent called menthol. *See* 683 F.3d at 1360-61,

see also id. 1364 (noting that prior art identified WS-3 and WS-23 as "the two most attractive cooling agents for commercial use from among 1200 cooling agents tested.") Both parties to the litigation were aware of this prior art; indeed, each party obtained its own patents directed to gum formulations incorporating one of those two compounds. *Id.* at 1358. Moreover—in an aspect of the opinion USL virtually ignores—the outcome in *Wrigley* relied on the fact that the inventors of the patent were simultaneously introduced to both WS-3 and WS-23 "during the same sales call, and they were told that the two compounds were appropriate for the same uses." *Id.* at 1366. But despite the fact that WS-23 and WS-3 were known beforehand to be interchangeable, the patent was drawn narrowly to WS-3 *See id.*

USL utterly fails in its attempt to shoehorn the present case into the facts of *Wrigley* solely by relying on the fact that the Dudley patent was distinguished in prosecution. (USL Br. at 24-25.) In stark contrast to the facts of *Wrigley*, Dudley discloses hundreds of individual penetration enhancers yet does *not* disclose the three-component enhancer system USL actually uses as the asserted equivalent. (*See supra* Part IV.A.2.a).) Moreover, as explained by Plaintiffs' expert, given the unpredictability of the field, there would have been no way to discern from Dudley that USL's enhancer system would have been interchangeable with the enhancers recited by the patents-in-suit. (Hadgraft Decl. ¶¶ 150-154.) Indeed, Plaintiffs'' expert explains that knowing the ingredients of USL's enhancer system would not be enough: [redacted] Thus, USL's argument does nothing more than identify yet another issue of material fact—whether the inventor of the patents-in-suit was on notice that the properties of USL's enhancer system made that combination a suitable substitute for oxa-2-one in the invention.

The present case is rather controlled by *Abraxis BioScience, Inc. v. Mayne Pharma Inc.*, 467 F.3d 1370, 1379-82 (Fed. Cir. 2006). In *Abraxis*, the issue was whether a compound called DTPA could be an equivalent to a structurally similar compound called edetate. *Id.* at 1379. The Federal Circuit held that, because there was no evidence in the record that DTPA was known to be a substitute for edetate, and because there was no disavowal in prosecution, there was no legal bar to the assertion of the doctrine of equivalents. *Id.* at 1381-82; *see also Wrigley*, 683 F.3d at 1366. Under USL's theory that "[n]arrow claims reciting specific members of a class of chemical compounds cannot be enlarged by the doctrine of equivalents to reach other chemical compounds" (USL Br. at 1), *Abraxis* would have reached the opposite result. In fact, *Abraxis* refutes USL's attempt to impose a *per se* limitation on the doctrine of equivalents.

Confirming the unsuitability of this argument for summary resolution, Judge Stark recently denied a generic manufacturer defendant's *Wrigley*-based motion for summary judgment for failure to show, as a matter of law, that the claim language in question was so "sharply narrowing as to require the exclusion of [the asserted equivalent] under the doctrine of equivalents." *AstraZeneca UK Ltd. v. Watson Labs., Inc.*, No. 10-915-LPS, __ F. Supp. 2d __, 2012 WL 5900706, at *3-5 (D. Del. Nov. 21, 2012).[17] After hearing *Wrigley*-based arguments from the generic company in that case, Judge Stark concluded that "the most appropriate course is to hear all of the evidence at trial and make a conclusion on the doctrine of equivalents thereafter." *Id.* Likewise here, USL's *Wrigley*-based argument presents disputed issues of material fact making summary judgment inappropriate.

[17] After Judge Stark denied summary judgment, the *AstraZeneca* parties conducted a 5-day bench trial. The case was recently resolved by settlement. *See* 10-915-LPS, D.I. 406-410, 424.

V. CONCLUSION

For the reasons set forth above and in the accompanying declarations, Plaintiffs respectfully request that Defendant's motion for summary judgment (D.I. 26) be denied in its entirety.

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